



**UNITED STATES DEPARTMENT OF COMMERCE  
Patent and Trademark Office**

Address: COMMISSIONER OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

KD

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
-----------------	-------------	----------------------	---------------------

08/945,459 12/09/97 MAKISHIMA

F 146.1275

BIERMAN MUSERLIAN AND LUCAS  
600 THIRD AVENUE  
NEW YORK NY 10016

HM12/0721

EXAMINER

ROMEO, D

ART UNIT

PAPER NUMBER

1646

DATE MAILED:

07/21/99

13

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trad marks**

# Office Action Summary

Application No.  
08/945,459

Applicant(s)

Makishima et al.

Examiner  
David S. Romeo

Group Art Unit  
1646



☒ Responsive to communication(s) filed on 4-16-99

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claims

☒ Claim(s) 1-7 and 9-16 is/are pending in the application.

Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

☐ Claim(s) \_\_\_\_\_ is/are allowed.

☒ Claim(s) 1-7 and 9-16 is/are rejected.

☐ Claim(s) \_\_\_\_\_ is/are objected to.

☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

## Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been  
☐ received.

☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Art Unit: 1646

### DETAILED ACTION

1. The amendment filed 04/16/99 (Paper No. 12) has been entered in full. Claims 1-7 and 10-16 are pending and are being examined.

2. Any objection or rejection of record that is not maintained in this Office action is  
5 withdrawn.

3. Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection.

4. Claim 15 remains rejected under 35 U.S.C. § 112, second paragraph, because it unclear what is intended by "arvecular" defects. The term does not appear to be commonly used or have  
10 a common and unambiguous meaning in the art and it is unclear what type of defects are intended. The metes and bounds are not clearly set forth.

### *Specification*

5. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the  
15 following is required: Applicants' should make an appropriate amendment of the specification so

Art Unit: 1646

as to have therein clear support or antecedent basis for the new term "alveolar" appearing in claim

7. This is necessary in order to insure certainty in construing the claims in the light of the specification, Ex parte Kotler 1901 C.D. 62; 95 O.G. 2684. See 37 CFR 1.75, MPEP § 608.01(i) and § 1302.01.

5

*New Claim Objections*

6. Claims 9, 10 and 16 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

10

Claim 9 has been interpreted as incorporating the limitations of claim 16.

Claim 9 is directed to a process of preparing the protein of claim 1 with a DNA encoding a polypeptide having the amino acid sequence of SEQ ID NO:1. The protein of claim 1 consist of the amino acid sequence of SEQ ID NO:1

15

Claim 10 is directed to a process of producing the protein of claim 2 with a DNA encoding a polypeptide having the amino acid sequence of SEQ ID NO:1. The protein of claim 2 consist of the amino acid sequence of SEQ ID NO:1.

A polypeptide having the amino acid sequence in SEQ ID NO:1 does not exclude additional, unrecited elements or amino acids because the transitional term "has" is inclusive or

Art Unit: 1646

open-ended. The transitional phrase "consisting of" excludes any element, step, or ingredient not specified in the claim. In re Gray, 53 F.2d 520, 11 USPQ 255 (CCPA 1931); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948)(consisting of defined as closing the claim to the inclusion of materials other than those recited except for impurities ordinarily associated therewith.).

5           Claim 16 is directed to a process of preparing the protein of claim 1 with a plasmid containing the nucleotide sequence of SEQ ID NO:4 having a part substituted with a DNA sequence having an ATG codon. SEQ ID NO:4 does not have an ATG initiation codon encoding methionine. The protein of claim 1 consist of the amino acid sequence of SEQ ID NO:1.

          A claim which depends from a claim which consists of the recited elements or steps cannot  
10   add an element or step. See M.P.E.P. 2111.03.

***New Claim Rejections - 35 USC § 112***

7.       Claims 9, 10 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

15   w/d       Claim 9 is rejected under 35 U.S.C. § 112, second paragraph, since it depends from a canceled claim, and thus makes no sense, since it is incomplete. In the interest of compact prosecution the claim will be interpreted as incorporating the limitations of claim 16. However,

Art Unit: 1646

this interpretation of the claim does not relieve applicant from the requirement to respond to the instant rejection.

w/d  
5 Claim 10 recites the limitation "the dimer protein according to claim 2" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. It is suggested that the claim recite "the protein according to claim 2".

n/d  
Claims 9 and 10 are ambiguous because the antecedent basis of the phrase "a methionine at the N-terminus" is unclear. It unclear whether the "polypeptide" or SEQ ID NO:1 has "a methionine at the N-terminus". The metes and bounds of the claim(s) are not clearly set forth.

w/d  
10 Claim 16 is indefinite over the recitation of "culturing the transformed" because it is unclear what is "transformed". It is suggested that the claim recite "culturing the transformed cells".

q  
15 Claim 16 is ambiguous because the antecedent basis of the phrase "encoded amino acid sequence" (lines 7) is unclear. It is unclear whether the phrase is referring to the "encoded amino acid sequence" of "a DNA sequence having an ATG initiation codon" or to the "encoded amino acid sequence" of "DNA sequence of SEQ ID NO:4". The metes and bounds of the claim(s) are not clearly set forth.

Claim 16 is indefinite over the recitation of "a part is substituted" (lines 4-5) because it is unclear which "part" is substituted. The metes and bounds of the claim(s) are not clearly set forth.

Art Unit: 1646

Claim 16 is indefinite over the recitation of "contains DNA sequence" because it is unclear whether the DNA sequence of SEQ ID NO:4 or some portion thereof is intended. The metes and bounds of the claim(s) are not clearly set forth.

***New Claim Rejections - 35 USC § 103***

5      8.      The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

9.      Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Celeste et al. (A) and Özkaynak et al. (U) in view of Ben-Bassat et al. (W), Tonouchi et al. (Y), Sherman et al. (V) and Georgiou (X).

10            Celeste et al. (A) teach a protein, MP52, which contains amino acids #1 to #120 of Celeste et al.'s. SEQ ID NO:4. Amino acids #2 to #120 of Celeste et al.'s. SEQ ID NO:4 are identical to applicants' SEQ ID NO:1. Celeste et al. also teach that the first cysteine of the seven cysteine domain of MP52 is encoded by the codon beginning at nucleotide #899 of SEQ ID NO:3 (column 7, full paragraph 3). The codon beginning at nucleotide #899 of SEQ ID NO:3 encodes  
15      amino acid #19 of SEQ ID NO:4. Celeste et al. also teach human MP52 proteins containing the amino acid sequence from amino acid #17 or #19 to #119 or #120 of SEQ ID NO:4 are expected to retain activity (column 7, full paragraph 3).

Art Unit: 1646

Applicants' SEQ ID NO:1 is the amino acid sequence of a mature protein in the TGF- $\beta$  superfamily.

Celeste et al. also teach that the MP52 protein appears to begin at nucleotide 845 off SEQ ID NO:3 and continues through nucleotide 1204 of SEQ ID NO:3 (column 7, full paragraph 2).

5 Celeste et al. teach that purified MP52 proteins may be produced by culturing a host cell transformed with a DNA sequence of SEQ ID NO:3 from nucleotide 845 to 1204 (column 7, full paragraph 3). Bacterial cells may also be suitable hosts (paragraph bridging columns 8-9). In producing MP52, according to the teachings of Celeste et al., one would express a protein with the N-terminal sequence Met-Ala-Pro-.

10 Özkaynak et al. (U) teach the N-terminal residues upstream of the 7-cysteine domains of the mature proteins in the TGF- $\beta$  superfamily (Figure 4) and teach that the mature N-termini of different members of the TGF- $\beta$  superfamily are quite diverse, that the N-termini have diverged because they are not crucial for receptor binding or protein folding, and that the N termini are not essential for biological activity (page 25226, column 2, full paragraphs 2-3).

15 One of ordinary skill in the art would reasonably expect that a protein consisting of the amino acid sequence of SEQ ID NO:1 would be biologically active because Celeste et al. teach that amino acid residues 1-18 can be deleted without affecting biological activity, as noted above. Furthermore, Özkaynak et al. teach that the N termini upstream of the 7-cysteine domains of the mature proteins in the TGF- $\beta$  superfamily are not essential for biological activity.



Art Unit: 1646

Celeste et al. and Özkaynak et al. do not explicitly teach or point to producing a protein consisting of the amino acid sequence in SEQ ID NO:1 by expressing a protein with the N-terminal sequence Met-Pro-.

Ben-Bassat et al. teach that in the case of Met-Ala-Pro-IL2, 60% of the bacterially  
5 expressed protein also lost the alanine residue, while no alanine removal was detected from the in vitro methionine aminopeptidase (MAP) reaction. Ben-Bassat et al. suggest that another aminopeptidase(s) might be responsible for the removal of the alanine residue. See page 735, paragraph bridging columns 1-2. Ben-Bassat et al. also suggest obtaining a homogeneous protein product without the N-terminal methionine (page 756, paragraph bridging columns 1-2).

10 Tonouchi et al. teach that the amino terminal residue of a bacterially expressed protein can be removed completely with aminopeptidase P (page 33, paragraph bridging columns 1-2).

Sherman et al. teach that when a foreign gene in bacteria was expressed at lower levels a N-terminal methionine could not be detected (page 29, column 3).

Georgiou teaches that the production of proteins that are identical to the natural product  
15 are highly desirable in the pharmaceutical industry, that the difference of a single amino acid residue can be deleterious to a patient receiving the protein and complicates approval of the product by the FDA (page 1240, paragraph bridging columns 1-2).

Ben-Bassat et al., Tonouchi et al., Sherman et al. and Georgiou do not teach a protein consisting of the amino acid sequence of SEQ ID NO:1.

Art Unit: 1646

One of ordinary skill in the art would reasonably expect that expressing a protein with the N-terminal sequence Met-Ala-Pro- in bacteria would result in a mixture of proteins with Met-Ala-Pro- and Pro- N-terminal residues, according to the teachings of Ben-Bassat et al. Accordingly, one of ordinary skill in the art would be motivated to bacterially express a protein consisting of the amino acid sequence of SEQ ID NO:1 with a methionine at the N-terminus, with a reasonable expectation of success, because this would result in the expression of a protein with the N-terminal sequence Met-Pro. One of ordinary skill in the art would be motivated to bacterially express such a protein with such an N-terminal sequence because one of ordinary skill in the art would have a reasonable expectation that a protein with the N-terminal sequence Met-Pro would be a single substrate of a single aminopeptidase, rather than a protein with the N-terminal sequence Met-Ala-Pro being the substrate of multiple amino peptidases, and a more homogeneous product with a Pro- at the amino terminus would be obtained. One of ordinary skill in the art would be motivated to obtain a homogenous product because Ben-Bassat et al. suggest doing so. A homogeneous product without an N-terminal methionine is also desirable from a pharmaceutical standpoint, as taught by Georgiou. Alternatively, a homogeneous gene product could be obtained with the aminopeptidase P of Tonouchi et al. Alternatively, a homogeneous gene product could be obtained by expressing the protein at lower levels, as taught by Sherman et al. The invention is prima facie obvious over the prior art.

Art Unit: 1646

10. Claims 1, 2 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Celeste et al. (A) and Özkaynak et al. (U) in view of Ben-Bassat et al. (W), Tonouchi et al. (Y), Sherman et al. (V) and Georgiou (X) as applied to claim 1 above, and further in view of Hötten et al. (2, cited by Applicants) and Cerletti et al. (N).

5 Celeste et al. and Özkaynak et al. in view of Ben-Bassat et al., Tonouchi et al., Sherman et al. and Georgiou teach a protein consisting of the amino acid sequence of SEQ ID NO:1, as discussed above.

Celeste et al. and Özkaynak et al. in view of Ben-Bassat et al., Tonouchi et al., Sherman et al. and Georgiou as applied to claim 1 above do not teach a protein consisting of the amino acid  
10 sequence of SEQ ID NO:1, wherein said protein is a homodimer, as recited in claim 2. Celeste et al. and Özkaynak et al. in view of Ben-Bassat et al., Tonouchi et al., Sherman et al. and Georgiou as applied to claim 1 above do not teach a process for preparing a protein consisting of the amino acid sequence of SEQ ID NO:1, wherein said protein is a homodimer, as recited in claim 10.

The teachings of Hötten et al. are of record. See the last Office action at page 4, line 14,  
15 through page 6, line 7. Specifically, Hötten et al. teach the amino acid sequence of a protein, GDF-5, comprising the amino acid sequence of SEQ ID NO:1. Hötten et al. teach that native GDF-5 is a dimer of the disulfide linked mature part of the protein as is seen in other members of the TGF- $\beta$  superfamily of proteins.

Art Unit: 1646

The teachings of Cerletti et al. are of record. See the last Office action at page 7, lines 1-6. In summary, Cerletti et al. teach a process for the production of biologically active, dimeric TGF- $\beta$ -like proteins.

5 Höttén et al. and Cerletti et al. do not teach a protein consisting of the amino acid sequence of SEQ ID NO:1, wherein said protein is a homodimer, as recited in claim 2. Höttén et al. and Cerletti et al. do not teach a process for preparing a protein consisting of the amino acid sequence of SEQ ID NO:1, wherein said protein is a homodimer, as recited in claim 10.

10 However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make a protein consisting of the amino acid sequence of SEQ ID NO:1 by bacterially expressing a protein consisting of the amino acid sequence of SEQ ID NO:1 with a methionine at the N-terminus, as taught by Celeste et al. and Özkaynak et al. in view of Ben-Bassat et al., Tonouchi et al., Sherman et al. and Georgiou as applied to claim 1, and to modify that teaching by making a protein consisting of the amino acid sequence of SEQ ID NO:1, wherein said protein is a homodimer, as taught by Höttén et al., with a reasonable expectation of  
15 success. One of ordinary skill in the art would be motivated to make this modification because native GDF-5 is a dimer of the disulfide linked mature part of the protein as is seen in other members of the TGF- $\beta$  superfamily of proteins.

It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to construct a plasmid containing DNA coding amino acid sequence in SEQ ID NO:1 of

Art Unit: 1646

the sequence listing with a methionine at the N-terminus, as taught by Celeste et al. and Özkaynak et al. in view of Ben-Bassat et al., Tonouchi et al., Sherman et al. and Georgiou as applied to claim 1 above, and further in view of Hötten et al. as applied to claim 2 above, and to modify that teaching by forming a dimer, as taught by Cerletti et al., with a reasonable expectation of success.

5 One of ordinary skill in the art would be motivated to combine these teachings in order to form a homodimer of GDF-5, the native form of the molecule.

The invention is prima facie obvious over the prior art.

11. Claims 1, 9 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Celeste et al. (A) and Özkaynak et al. (U) in view of Ben-Bassat et al. (W), Tonouchi et al. (Y), Sherman et al. (V) and Georgiou (X) as applied to claim 1 above, and further in view of Sambrook et al. (Z), Hsiung et al. (UU), and Gelfand et al. (B).

Celeste et al. and Özkaynak et al. in view of Ben-Bassat et al., Tonouchi et al., Sherman et al. and Georgiou teach a protein consisting of the amino acid sequence of SEQ ID NO:1, as discussed above.

15 Celeste et al. and Özkaynak et al. in view of Ben-Bassat et al., Tonouchi et al., Sherman et al. and Georgiou do not teach a process for preparing the protein comprising constructing the plasmid recited in claim 16, wherein said plasmid contains a DNA encoding said polypeptide with a methionine at the N-terminus.

Art Unit: 1646

Sambrook et al. teach increasing the expression of foreign genes in bacteria by using site directed mutagenesis to increase translation initiation. Translation initiation can be increased by removal of potential secondary structure involving the ribosome binding site. Changing the sequence near the SD and ATG sequences may increase expression. See page 17.36.

5           Hsiung et al. show that replacing the 5' terminal codons with A-T-rich codons enhances the expression level of a foreign gene in bacteria (page 390, full paragraph 2). Hsiung et al. suspected that mRNA transcribed from the foreign gene might form secondary structures that inhibited translation. The first eight codons of the foreign gene were, therefore, changed to A-T-rich codons, and the expression level of the foreign gene was increased. See page 397, full  
10       paragraph 3.

Gelfand et al. teach oligonucleotide-directed mutagenesis to increase the A/T content of four of the first seven codons without effecting a change in the encoded amino acids of a foreign gene expressed in bacteria (column 39, last paragraph).

15           Sambrook et al., Hsiung et al., and Gelfand et al. do not teach a process for preparing the protein comprising constructing the plasmid recited in claim 16, wherein said plasmid contains a DNA encoding said polypeptide with a methionine at the N-terminus.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make a protein consisting of the amino acid sequence of SEQ ID NO:1 by bacterially expressing a protein consisting of the amino acid sequence of SEQ ID NO:1 with a

Art Unit: 1646

methionine at the N-terminus, as taught by Celeste et al. and Özkaynak et al. in view of Ben-Bassat et al., Tonouchi et al., Sherman et al. and Georgiou, and to modify that teaching by increasing the A/T content around the ATG codon, with a reasonable expectation of success.

One of ordinary skill in the art would be motivated to make this modification in order to increase the expression level of the encoded protein and thereby obtain more of the protein. The invention is prima facie obvious over the prior art.

12. Claims 1-7 and 11-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Celeste et al. (A) and Özkaynak et al. (U) in view of Ben-Bassat et al. (W), Tonouchi et al. (Y), Sherman et al. (V) and Georgiou (X) as applied to claim 1 above, and further in view of Hötten et al. (2, cited by Applicants) and Cerletti et al. (N) as applied to claim 2 above, and further in view of Neidhardt et al. (1, cited by Applicants), Adams et al. (C), and Ethridge (D).

Celeste et al. and Özkaynak et al. in view of Ben-Bassat et al., Tonouchi et al., Sherman et al. and Georgiou as applied to claim 1 above, and further in view of Hötten et al. and Cerletti et al. as applied to claim 2 above, teach a protein consisting of the amino acid sequence of SEQ ID NO:1, wherein said protein is a homodimer, as discussed above.

Celeste et al. and Özkaynak et al. in view of Ben-Bassat et al., Tonouchi et al., Sherman et al. and Georgiou as applied to claim 1 above, and further in view of Hötten et al. and Cerletti et al. as applied to claim 2 above do not teach a pharmaceutical composition comprising a protein

Art Unit: 1646

consisting of the amino acid sequence of SEQ ID NO:1, wherein said protein is a homodimer, and a pharmaceutically acceptable carrier. Celeste et al. and Özkaynak et al. in view of Ben-Bassat et al., Tonouchi et al., Sherman et al. and Georgiou as applied to claim 1 above, and further in view of Hötten et al. and Cerletti et al. as applied to claim 2 above do not teach do not teach  
5 administering such a pharmaceutical composition to a human in an amount effective to treat the recited cartilage or bone diseases.

The teachings of Neidhardt et al. are of record. See the last Office action at page 8, line 3, through page 10, line 2. Specifically, Neidhardt et al. teach a pharmaceutical composition comprising MP52 and a pharmaceutically acceptable carrier for use in the healing of bone,  
10 cartilage, or tooth defects and discloses the administration of such a composition to humans (page 9, full paragraph 1).

Adams et al. teach inducing bone formation for the treatment of bone fracture, osteoporosis, and osteoarthritis (column 5, full paragraph 4).

Ethridge teaches inducing bone formation for the treatment of alveolar defects (column 7,  
15 full paragraph 2; claim 28).

Neidhardt et al., Adams et al., and Ethridge do not teach a pharmaceutical composition comprising a protein consisting of the amino acid sequence of SEQ ID NO:1, wherein said protein is a homodimer, and a pharmaceutically acceptable carrier. Neidhardt et al., Adams et al., and



Art Unit: 1646

Ethridge do not teach do not teach administering such a pharmaceutical composition to a human in an amount effective to treat the recited cartilage or bone diseases.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make a protein consisting of the amino acid sequence of SEQ ID NO:1, wherein said protein is a homodimer, as taught by Celeste et al. and Özkaynak et al. in view of Ben-Bassat et al., Tonouchi et al., Sherman et al. and Georgiou as applied to claim 1 above, and further in view of Hötten et al. and Cerletti et al. as applied to claim 2 above, and to modify that teaching by making a pharmaceutical composition comprising the homodimer and a pharmaceutically acceptable carrier, and to administer such a pharmaceutical composition to a human in an amount effective to treat bone, cartilage, or tooth defects, as taught by Neidhardt et al., Adams et al. and Ethridge with a reasonable expectation of success. One of ordinary skill in the art would be motivated to combine these teachings because Neidhardt et al., Adams et al. and Ethridge teach that such a composition would useful for such purposes. The invention is prima facie obvious over the prior art.

### *Conclusion*

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Art Unit: 1646

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Art Unit: 1646

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David S. Romeo whose telephone number is (703) 305-4050. The examiner can normally be reached on Monday through Friday from 6:45 a.m. to 3:15 p.m.

5 If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached on (703) 308-4310.

Official papers filed by fax should be directed to (703) 308-4242.

Faxed draft or informal communications should be directed to the examiner at (703) 308-0294.

10 Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

*Elizabeth C. Kemmerer*

ELIZABETH KEMMERER  
PRIMARY EXAMINER

dsr *dsr*  
July 17, 1999